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Improvement in pelvic pain with botulinum toxin type A – Single vs. repeat injections

E.M. Nesbitt-Hawes [a,b,*], H. Won [a,b], S.K. Jarvis [a,b], S.D. Lyons [a,b], T.G. Vancaillie [a,b], J.A. Abbott [a,b]

[a] Department of Endo-Gynaecology, Royal Hospital for Women, Sydney, Australia
[b] University of New South Wales, Sydney, Australia

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ABSTRACT

The aim of this prospective study was to report the outcomes of pain and vaginal pressures of successive botulinum toxin type A injections for women with objective pelvic floor muscle overactivity and a two-year history of pelvic pain. Between 2005 and 2008, 37 women underwent injection of 100 IU of botulinum toxin type A into the puborectalis and pubococcygeous muscles with dysmenorrhoea, dyspareunia, dyschesia, and non-menstrual pelvic pain assessed using a visual analogue scale (VAS), and vaginal pressure measured by vaginal manometry, at 0, 4, 12 and 26 weeks from each injection. 26 women (70%) had one injection of botulinum toxin type A and 11 (30%) had 2 or more injections. The second injection was performed at the earliest at 26 weeks after the first, with subsequent injections having a median time to re-injection of 33.4 weeks (range 9.4–122.7 weeks). Single and repeated injections both demonstrated a statistically significant reduction in dyspareunia by VAS scores from 54 to 30 in the single injection group and from 51 to 23 in the multiple injection group ($p = .001$), non-menstrual pelvic pain VAS from 37 to 25 ($p = .04$), as well as vaginal pressures; 40 versus 34 cm H_2O ($p = .02$). No statistically significant difference in dysmenorrhoea or dyschesia was observed for either group from their baseline scores. Multiple injections of botulinum toxin type A in women with pelvic floor muscle overactivity provide significant relief from dyspareunia and non-menstrual pelvic pain. The upper limit between re-injection is not yet determined, nor is the maximum number of treatments. Clinical outcomes for single and subsequent injection of botulinum toxin type A for recurrent pelvic pain are equivalent. Women who have had benefit from a single injection of botulinum toxin type A can be reassured that if symptoms reoccur, repeated injections can be expected to be equally efficacious.

1. Introduction

Botulinum toxin type A produces localised muscle weakness or paralysis through biochemical denervation and is used for the treatment of many neuromuscular disorders, as well as chronic pelvic pain and pelvic floor overactivity (Jankovic and Brin, 1991; Maria et al., 2000; Abbott, 2009; Bjornson et al., 2007). Reduction in pain is associated with a return to normal physical activity, mood and quality of life (Stones et al., 2000). Clinical effects are often seen within 1 week of injection, and benefits typically last from 3 to 6 months. Multiple dosing is utilised to extend the treatment effect and has been demonstrated to be beneficial in neuromuscular disorders, muscle spasticity and detrusor overactivity (Bakheit et al., 2001).

There are limited data on the long-term effects of recurrent dosing with botulinum toxin type A, however there is concern with regards to potential toxicity, antibody

* Corresponding author. Department of Endo-Gynaecology, Royal Hospital for Women, Barker St, Randwick, NSW 2031, Australia. Tel.: +61 2 93826111; fax: +61 2 93826246.
E-mail address: erin.nesbitt-hawes@sesiahs.health.nsw.gov.au (E.M. Nesbitt-Hawes).

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formation and secondary failure of botulinum toxin type A treatment (Lange et al., 2009). Given the proximity of pelvic sphincters to the injection site for gynaecological applications of botulinum toxin type A, the effects of long-term muscle wasting and remodelling on both target- and non-target muscles is critical in the evaluation of this treatment (Fortuna et al., 2011).

Our unit has previously conducted a series of studies demonstrating that the use of botulinum toxin type A improved pelvic pain and vaginal pressures in women with pelvic floor muscle hypertonicity (Abbott et al., 2006; Jarvis et al., 2004). This study aims to report the longitudinal outcomes for repeat injections of botulinum toxin type A into the pelvic floor muscles of women with objective pelvic floor muscle overactivity, as well as the interval to re-injection, pain outcomes and vaginal pressures with repeated injections.

2. Materials and methods

This is a prospective cohort study carried out at the Department of Endo-Gynaecology, Royal Hospital for Women, Sydney, Australia. This study received approval from the institutional scientific and ethics committees (HREC ref 03/102).

2.1. Eligibility

Between August 2005 and December 2008, women aged between 18 and 55 years with a minimum two-year history of pelvic pain and who had previously completed either the pilot study or the randomised controlled trial (RCT) were invited to participate. Eligibility criteria included documented pelvic floor overactivity with at least two of the following: pelvic floor myalgia on palpation; vaginal manometry reading of greater than 40 cm H_2O; or chronic pelvic pain. Willingness to attend follow-up and compliance with the study protocol were essential. Study participants were consented following the receipt of written information and the opportunity to ask research staff study-related questions.

2.2. Exclusion criteria

Exclusion criteria included: current pregnancy or desire for pregnancy in the six months following injection; inability to tolerate vaginal pelvic floor muscle examination and manometry; breast feeding; or those not willing to use a reliable method of contraception. Women with a known contraindication for the use of botulinum toxin type A, those with history of neuromuscular and/or bleeding disorders were excluded, as well as those who were using aminoglycoside antibiotics or had poor comprehension of written and spoken English.

2.3. Data collection

Participating women were asked to complete demographic data and underwent full medical history and detailed examination. Assessment of pain was performed by visual analogue scale (VAS) with separate scores obtained for dysmenorrhoea, dyspareunia, dyschesia, and non-menstrual pelvic pain. Pelvic floor pressure was measured by vaginal manometry via an air-filled vaginal probe (Peritron; Cardio Design, Melbourne, Australia). Recorded assessments included resting pressure and maximum contraction pressure.

2.4. Botulinum toxin A injection procedure

The injection procedure has been previously described (Jarvis et al., 2004) and is summarised here. Under conscious sedation monitored by an anaesthetist, the pelvic floor muscles were examined vaginally and 100 IU of botulinum toxin type A (BOTOX, Allergan Westport, Ireland) diluted in 4 ml of normal saline was injected into two sites bilaterally within each of the puborectalis and pubococcygeous muscles in divided doses. Women recovered for 1–2 h until they could eat, drink, mobilise, and void. Initial follow-up was by telephone call 2–3 days after injection, and post-procedure reviews were performed at 4, 12 and 26 weeks from each injection. At each follow-up, study participants completed VAS scores for pain and were examined to assess pelvic floor tenderness and record vaginal manometry.

2.5. Patient groups

Women in the single injection group came from the placebo group of patients in the RCT and were botulinum toxin type A naïve. During the study period, these women may not have received a second injection due to complete resolution of symptoms; no improvement with the first dose of botulinum toxin type A; or desire not to continue with further dosing. This group was used as the comparator for the multiple injection group. After injection, routine follow-up was not extended beyond 26 weeks.

Repeat injections of botulinum toxin type A were offered to women who had a good clinical response to the index injection with changes in pain symptomatology. Recurrence of pelvic pain and clinical signs of pelvic floor myalgia on palpation determined the timing of re-injection. Women who had repeat injections followed the same protocol used for the initial injection and returned for timed follow-up to assess the effect of each subsequent injection.

2.6. VAS scores

Changes in VAS scores for pain and vaginal pressures were assessed in each of the single and multiple injection groups over the follow-up period. A comparison between the single and repeat injection groups was also made to determine if repeated botulinum toxin type A dosing continues to be effective.

2.7. Statistical analysis

Statistical analyses were performed using SPSS 20.0 (SPSS Inc, Chicago, IL). The Kolgarov–Smirnov test was performed to determine the distribution of data. Baseline to 26 week post-treatment data was compared using the Freidman test for multiple dependent non-parametric data.